BACTERICIDAL COMPOSITIONS

Patent Number: GB1488891

Publication date: 1977-10-12

Inventor(s):

Applicant(s): ROHM & HAAS

Requested Patent: GB1488892

Application Number: GB19740046007 19741024

Priority Number (s): US19730426881 19731220

IPC Classification: A61L13/00

EC Classification: A01N43/80

Equivalents: CA1036070, DE2459446, DK668574, FR2255083, IT1024896, JP50095429, SE430119, SE430373, SE7415860, SE7710162

Abstract

1488891 Isothiazolone / quaternary am- monium salt compositions ROHM & HAAS CO 24 Oct 1974 [20 Dec 1973] 46007/74 Heading A5E A bactericidal composition contains a 3- isothiazolone and a bactericidal quaternary ammonium salt, wherein the 3-isothiazolone is (a) a compound of the formula: wherein Y is (1) an optionally substituted alkyl group (other than aralkyl), (2) a cyclo- alkyl group, (3) an optionally substituted aralkyl group or (4) (except in the case where R and R' each represent chlorine) an op- tionally substituted aryl group, R is a hydro- gen atom, a halogen atom, or an optionally substituted alkyl group; and R' is a hydrogen atom, a halogen atom, or an optionally sub- stituted alkyl group, (b) a salt of a compound of Formula I with an acid or (c) a metal salt complex of a compound of Formula I. The quaternary ammonium salt may be a di (C 1 -C 4) alkyl (C 8 -C 18) alkyl benzyl am- monium halide. The compositions find ap- plication as disinfectants in swimming pools and other aqueous systems, and in treating surfaces soiled with organic matter such as faeces, e.g. chicken and turkey coops, barns, sties and dairies. Specification 1488892 is referred to.

Description

(54) BACTERICIDAL COBOSsITIES
(71) We, ROHM AND HAAS COM
PANY, a corporation orgarused under the laws of the State of Delaware, United States of America, of Independence Mall West, Philadelphia, Pennsylvania 19105, United States ob America, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:-
This invention relates to bactericidal com- positions.

Quaternary ammonium compounds, especially those having at least one strongly hydrophobic substituent, are widely used as sanitizing and disinfecting agents. However, these compounds are generally greatly inactivated by the presence of organic matter and by common organic additives, rhus minimizing their effectiveness, (and, indeed, contra-indicating their use when rapid inactivation takes place) in treating soiled surfaces, in imparting residual activity to easily soilable surfaces, and in protecting formulated products from bacterial attack.

The present invention provides a bactericidal composition containing a 3-isothiazolone as specified below and a bactericidal quaternary ammonium salt
In tests which have been carried out on compositions according to the invention, rhe compositions were resistant to inactivation by organic mater and organic additives and exhibited a synergistic increase in microbicidal activity. Many compositions according to the invention also show unexpected residual activity, even on soiled surfaces.

The 3-isothiazolones which are used in the compositions of the invention, are (1) 3-isothiazolones of the formula

Formula (I) wherein
Y is an optionally substituted alkyl group (other than aralkyl which is specifically listed below), preferably one having 1 to 18 carbon atoms, a cycloalkyl group, prefer ably having 3 to 8 carbon atoms in the ring, an optionally substituted aralkyl group, pre ferably having up to 10 carbon atoms (e.g.

benzyl), or (except in the case where R and R' each represent chlorine) an option ally substituted aryl group, preferably having up to 10 carbon atoms (e.g. phenyl);
R is a hydrogen atom, a halogen atom, prefer ably chlorine or bromine, or an optionally substituted alkyl group, preferably having 1 to 4 carbon atoms; and
R' is a hydrogen atom, a halogen atom, pre ferably chlorine or bromine, or an optionally substituted alkyl group, preferably having 1 to 4 carbon atoms; (2) salts of compounds of Formula I with an acid, such as hydrochloric acid, hydrobromic acid, perchloric acid, nitric acid, sulfuric acid, oxalic acid, trichloroacetic acid or p-toluene sulfonic acid, and (3) metal salt complexes especially of the formula

Formula (II) wherein
Y, R, and R' are as defined above,
M is a cation of a metal or a cationic complex
of a metal, such as barium, cadmium,
calcium, chromium, cobalt, copper, iron,
lead, lithium, magnesium, manganese, mer
cury, nickel, sodium, silver, strontium, tin
or zinc;
X is an anion forming a compound with the
cation M, wherein the compound has suf
ficient solubility to form a metal salt com
plex;; a is the integer 1 or 2; and n is an integer which for the anion X satisfies
the valence of the cation M
When the 3-isothiazolones contain a substituted alkyl group one or more hydrogen atoms in the alkyl group may be replaced and the substituted alkyl group may be hydroxyalkyl, haloalkyl, cyanoalkyl, alkylaminealkyl, dialkylaminoalkyl, arylaminoalkyl, carboxyalkyl, carbalkoxyalkyl, alkoxyalkyl, aryloxyalkyl, alkylthioalkyl, arylthioalkyl, isothiazolonylalkyl, haloalkoxyalkyl, carbamoxyalkyl, aza cycloalkylalkyl, such as morpholinoalkyl, piperidinoalkyl or pyrrolidonylalkyl.

In the case of substituted aralkyl groups, such as substituted benzyl, phenethyl, methylbenzyl, there may be used aralkyl groups having one or more of the hydrogen atoms on either the aryl ring or the alkyl chain replaced by another substituent group. Examples of the substituted aralkyl groups which may be present in 3-isothiazolones and the metal salt complexes of Formulas I and II include halogen- nitro, (C1-C4)alkyl-, or (C1-C4)- alkoxy-substitated aralkyl groups.

In the case of substituted aryl, e.g. phenyl, naphthyl, or pyridyl, there can be used aryl groups having one or more of the hydrogen atoms on the aryl ring replaced by another substituent such as halogen, cyano, nitro, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)alkylacylamino, (C1-C4)carbalkoxy or sulfamyl.

Representative Y substituents include hydrogen, methyl, ethyl, propyl, isoporpyl, butyl, hexyl, octyl decyl, pentadecyl, octadecyl, cyclopropyl, cyclohexyl, benzyl, 3,4 dichlorobenzyl, 4-methoxybenayl, 4-chloro-
benzyl, phenyl, 3,4-dichlorophenyl, 4-methoxy
phenyl, naphthyl, hydroxymethyl, chloro
methyl, chloropropyl, diethylaminoethyl,
cyanoethyl, carbomethoxyethyl, ethoxyethyl, 2 - methoxy - 1 - bromoethyl, 3,3,5 - trimethyl cyclohexyl, phenoxyethyl, p - chloroanilino-
methyl, phenylcarbamoxymethyl, hydroxy
butyl, carboxyethyl and 1-isothiazolonylethyl.

Representative R and R' substituents include
hydrogen, bromine, chlorine, iodine, methyl,
ethyl, propyl, isopropyl, butyl, and t-butyl.

The alkyl substituents represented by Y, R,
and R' can have either branched- or straight
chain spatial configuration.

Among the anions which X can represent
are chloride, bromide, iodide, sulfate, nitrate,

nitrite, acetate, chlorate, perchlorate, bisulfate, bicarbonate, oxalate, maleate, p-toluene sulfonate, carbonate and phosphate. The pre ferred metals from which M is derived are calcium, copper, magnesium, manganese, nickel, and zinc. Among the metal cations embraced by M are cationic complexes of the metal ions, including complexes with ammonia, simple organic amines, and various hetero cyclic organic amines such as pyridines or pyrimidines.

The preparation and properties of the 3-isothiazolones and metal salt complexes usable in the invention are described in French Patent Specification Nos. 7031977, and 7216789, and United States Patent Nos.

3,517,022, 3,544,480 and 3,761,488.

A sub-class of 3-isothiazolones of interest are those in which Y is (C:-) alkyl, (C,-C8)cycioalkyl, phenyl or benzyl each optionally substituted by halogen, R is hydrogen, halogen or (C1-C4) alkyl and R' is hydrogen or halogen.

A particularly useful group of 3-isothiazolones are those in which R is a methyl group or a halogen atom, preferably a bromine or chlorine atom and R' is a halogen atom, preferably a bromine or chlorine atom. In this group, those compounds in which Y is a substituent having three to eight carbon atoms, and preferably six or seven carbon atoms, such as a hexyl group, a cyclohexyl group, a phenyl group, a halophenyl group, a nitrophenyl group, a benzyl group, or a halobenzyl group, are generally most active, especially in pro viding good residual activity.

The quaternary ammonium saws which can be used are well-known compounds, and in clude di(C1-C)alkyl, (C8-C18)alk'A benzyl ammonium halides, such as dimethyldodecyl benzylammonium chloride, diethyldodecyl-benzylanunonium chloride; p-diisobutyl phenoxyethoxyethyldimethylbenzylammonium chloride;Benzalkon B (dimethyl higher alkyl dichlorobenzyl ammonium chloride) and dimethylocatdecylidmethylbenzl ammonium chloride; alkyldimethylethylbenzylammonium halides; di(lower alkyl) di(higher alkyl) ammonium halides and tri(lower alkyl) higher alkyl ammonium halides, such as dimethyldidecylammonium chloride, dimethyldidodecylammonium chloride and trimethyltetradecyl- ammonium chloride; methyldiethyldecyloxyethyl ammonium bromide; methyldodecylbenzyltrimethylammonium chloride; methyl d o d e c y l xylylenebis(trimethyl)ammonium chloride; N-trirnethyl-N-chloro-N'-benzyl-N' - dodecylglycinamide;N - (higher alkyl)heterocyclics such as cetylpyridinium chloride, 2-tridecylpyridinium sulfate, 1-hexadecyl- pyridinium chloride, 2-dedecylisoquinolmium bromide, 2-octyl- 1 - (2-hydroxyethyl) imidazo- linium chloride, 6-dodecy1Oxybenzylqulino- linium chloride, and benayldecylpiperidinium chloride.

Mixtures of these quaternary ammonium salts can also be used. The preferred quaternary ammonium salts are those having at least one hydrophobic chain of 8 to 18 carbon atoms, most particularly the n-alkyldimethyl- benzyl anunonium halides, including mixtures of C12-, C14-, and C1-alkyl dimethylbenzyl ammonium halides and substituted-benzyl ammonium halides.

The ratio of 3-isothiazotone to quaternary ammonium salt and the use levels thereof can be varied greatly depending on the degree of total activity desired, the degree of bacterial contamination to be eradicated, the quantity of organic matter present or to be expected, the nature of the area or surface to be treated, the quaternary ammonium salt and isothiazolone involved, and related factors. Generally, the weight ratio of 3-isothiazollone (including, of course, the salts and metal complexes od compounds of Formula I) to quaternary ammonium salt will be from 5:1 to 1:50, preferably 1:1 to 1:15 and most preferably 1:2 to 1:7. The upper limits for each of the active components are usually related to purely economic considerations.However, when used as disinfectants rather than as germicides, higher relative levels of the quaternary ammoi nium salts are generally preferable.

The 3 -isothiazolone and quaternary compound can be formulated in any convenient fashion using appropriate solvents such as water, alcohols and glycols, or mixtures of solvents. For various use applications, it may be advantageous to add suitable surfactants, as well as other conventional additives such as synthetic liquid or solid detergents, stabilizers, anticorrosive agents or extenders. The compositions can be formulated at any desired concentration, the choice of concentration generally being dependent on the particular use conditions which may be anticipated. In general, the compositions will be applied to the locus to be treated at a formulated concentration of about 50 to about 1000 parts per million by weight of quaternary ammonium compound and about 1/2 to about 200 parts per million by weight of 3-isothiazolone.However, it should be noted that in some applications, such as for example swimming pools and other aqueous systems, much lower levels, even down to 1 to 2 parts per million, of the quaternary compound may be used.

The compositions of the invention can be used as sanitizers, germicides, and disinfectants in many different applications, on many different surfaces, and in many different environments. These compositions are particularly useful in treating surfaces which have become soiled with organic matter, particularly animal faeces, and in providing relatively lasting germicidal protection to environments, being soiled surfaces such as those of chicken and turkey coops, barns, sties and dairies, which can become quickly soiled after initial application of the compositions. The activity of the compositions is greater than would be expected from the combined individual activity of the 3-isothiazolone and quaternary compound. The synergistic activity can be seen in many different ways. For example, in the presence of levels ob organic matter which essentially inactivate the quaternary ammonium salt, the combination of quaternary compound with 3-isothiazolone possesses greater activity than the 3-isothiazo lone alone. Additionally, the combination of quaternary ammonium salt and 3-isothiazol- lone can provide more rapid germicidal action or greater residual activity in the presence of organic matter than either the quaternary or the 3-isothiazolone alone at the same concentrations.

The following examples will further illus
trate the present invention but are not in
tended to limit it in any way. All temperatures are in degrees Centigrade and percentages and parts are by weight, unless otherwise stated.

Example I.

To determine the bactericidal effectiveness of the compositions of the invention, the following time-survival test proceduxe is followed.

At zero time 10 ml. od stock bactericide solution (10 times the desired use concentration) are added to 90 ml of distilled water containing 1 ml. ob a 24-hour broth culture of the test organism, plus the desired concentration of sterile, dried, ground, poultry manure. The test container is shaken vigorously to give thorough mixing of the contents.

At each of the selected exposure times, 1 ml. of the mixture is removed from the test container

and placed in a 9 ml. inactivator blank containing sufficient inactivator to inactivate the highest concentration of each of the bactericides under test. In the tests described herein a mixture d 0.2% lecithin, 1.6%
Tween-80 (Tween is a registered trade mark), and 0.05% sodium thioglycollate is employed as the inactivating solution.

After thorough mixing, either 1 ml. or serial dilutions of the test solution-inactivating solution mixture are plated with T.G.E. Agar (i.e.

Tryptone-Glucose-Extract Agar) containing additional inactivating mixture.

The above steps are carried out at 25 C.

The plates are incubated for 48 hours at 370C and then observed for numbers of surviving organisms.

The test organism used is Escherichia coli (E. coli No. 11229). The test bactericides are
Q-n - alkyl)C14: 50%; C12: 40%; C16:
10%) dimethylbenzylammonium chlor
ide
Q-a mixture of 50% by weight alkyl
(C14: 60%; C16: 30%; C12: 5%; C18:
5 %) dimethylbenzylammonium chlor
ide and 50% alkyl (C12: 50%; C14:
30%; C16: 17%; C1: 3%) dimethyl
ethylbenzylammonium chloride
Q3-a mixture of (n-C8 to n-C18)alkyldi-
methylb-enzylammonium chlorides con
tailing not less than 40% by weight
n-Cl2 alkyl; not less than 20% n-Cl4
alkyl and not less than 70% by weight
total of n-C12 and n-C14 alkyl. Com
mercially available under the regis
tered trademark Roccal for Sterling
Drug Corporation
R4-p - diisobutylphenoxyethoxyethyldi
methylbenzylammonium chloride
Q5-a mixture of 80% by weight of methyl
d o d e c y lbenzyltrimethylammonium
chloride and 20% of methyldodecyl
x y l y l e ebis(trimethyl)ammonium
chloride
I1-calcium chloride complex of 5-chloro
2-methyl-3-isothiazolone
I2 4,5 - dichloro - 2 - cyclohexyl - 3
isothiazolone
Table I summarizes typical results of these tests.

TABLE I
Time Survival Test
No. of Organisms/ml. of Test Solution After
Germicide (conc-ppm) Organic Matter* 5min. 10min. 30min. 24 hrs. 48hrs. 1wk. Q (50 ppm) none
- 0 0 0 -
Q (50 ppm) 0.25% TNTC** TNTC TNTC TNTC TNTC TNTC
Q (50 ppm) 1% - TNTC TNTC TNTC -
Q (400 ppm) 1% - 182 189 TNTC -

Q (50 ppm) + I1 (50 ppm) 1% - TNTC TNTC 15600 -
Q (100 ppm) + I1 (50 ppm) 1% - TNTC TNTC 3640 -
Q (200 ppm) + I1 (50 ppm) 1% - 43500 20150 0 -
Q (400 ppm) + I1 (50 ppm) 1% - 403 105 0 -
Q (50 ppm) + I2 (50 ppm) 1% - 12700 314 0 -
Q (100 ppm) + I2 (50 ppm) 1% - 3510 75 0 -
Q (200 ppm) + I2 (50 ppm) 1% - 281 0 0 -
Q (400 ppm) + I2 (50 ppm) 1% - 5 0 0 -
Q (50 ppm) + I2 (25 ppm) TNTC TNTC 2210 0 0 0
Q (50 ppm) + I2 (12.5 ppm) TNTC TNTC > 10000 0 0 0
Q (50 ppm) + I2 (6.25 ppm) 0.25% TNTC TNTC TNTC 0 0 0 TABLE I (Continued)
No. of Organisms ml. of Test solution After
Germicide (conc ppm) Organic Matter* 5 min. 10 min. 30 min. 24 hrs. 48 hrs. 1 wk
Q1 (50 ppm) + 12 (3.13 ppm) 0.25% TNTC TNTC TNTC 0 0 0
Q1 (50 ppm) + 12 (1.5 ppm) 0.25% TNTC TNTC TNTC 1 0 0
Q1 (50 ppm) + 12 (0.8 ppm) 0.25% TNTC TNTC TNTC 32 1 0
Q1 (50 ppm) + 12 (0.4 ppm) 0.25% TNTC TNTC TNTC 10,000 TNTC TNTC
Q1 (50 ppm) + 12 (0.2 ppm) 0.25% TNTC TNTC TNTC TNTC TNTC TNTC
Q2 (50 ppm) 0.25% 46800 19500 TNTC -
Q3 (50 ppm) 0.25% TNTC TNTC TNTC -
Q4 (50 ppm) 0.25% - TNTC TNTC TNTC -
Q5 (50 ppm) 0.25% - TNTC TNTC TNTC -
Q2 (50 ppm) + 12 (50 ppm) 0.25% 4940 72 0
Q3 (50 ppm) + 12 (50 ppm) 0.25% 37700 910 0 -
Q4 (50 ppm) + 12 (50 ppm) 0.25% TNTC 52650 0 -
Q5 (50 ppm) + 12 (50 ppm) 0.25% TNTC 9750 0 - *Sterile dried ground poultry manure **TNTC surviving organisms too numerous to count (100,000) Example II.

The following use-dilution test, run at 20 C, is also used to evaluate the bactericidal effectiveness of the compositions of the invention, using test baotericides named in Example i.

Five stainless stell rings contaminated in the usual manner with a 48-hour broth culture of Salmonella chloreraesuis are dried for onehalf hour at 37 C and then added to five replicate medication tubes containing sterile, dried, ground chicken manure. At zero time, 10 ml. of the test solution is added to the first tube containing the ring and manure, and then to each of the nine remaining tubes, at 30-second intervals.

After one hour exposure to the test solution, the rings are removed at 30-second intervals from five of the ten replicate tubes. As each ring is removed from the test solution, it is placed in another tube containing 10 ml. of sterile inactivator solution (0.2% lecithin, 1.6% Tween-80 and 0.05% sodium thioglyoollate).

The inactivator tubes containing the rings are then spun vigurously on a Vortex Mixer to suspend the surviving organisms and 1 ml., 0.1 ml., 10-2 and 10-3 dilutions of the resulting suspension are plated with T.G.E. Agar containing inactivator. These plates are also incubated for 48 hours at 37 C.

After all plates have been incubated for 48 hours, they are examined to determine the number of colonies present. These figures are then used to calculate the number of surviving organisms per ring.

Table II summarizes typical results of these tests.

TABLE II
Use-Dilution Test
No. of Organisms Surviving Ring After

Germicide (conc-ppm) Organic Matter 1 hr. 24 hrs. 48 hrs.

Q (50 ppm) 0.25% 8000 36000 3,800,000
Q (50 ppm) + 11 (25 ppm) 0.25% 2580 - < 10
Q (50 ppm) + 12 (75 ppm) 0.25% < 10 < 10 < 10 Example III.

The following test procedure is followed to evaluate the residual bactericidal activity of the compositions of the invention, using the test germicides named in Example I.

A sufpension of sterile dried polultry manure in a 24-hour broth culture of Staphylococecus aureus or Enterobacter aerogenes is applied to the upper surface of a sterile glass microscope slide. The suspension is then dried on the slide at 37 C for 1 hour.

Exactly 0.2 ml. of test solution is applied to the contaminated surface of the slide and spread out by means of a wire loop.

The treated slides are placed in a humidity chamber at 25 C and 87% relative humidity for the desired exposure times. At the end of the indicated exposure times, the slides are placed in sterile perri and covered with 20 ml. of inactivator soution (0.1% lecithin, 0.7% Tween-80 and 0.05% sodium thioglycollate). The slides are thoroughly scraped by means of a rubber policeman to remove and suspend surviving organisms. Serial dilutions of the resulting suspension are then plated with T.G.E. Agar containing additional inactivator. All plates are incubated at 37 C for 24 or 48 hours. Following incubation, the Agar plates are observed for numbers of bacterial colonies and these numbers are employed to calculate the number of organisms surviving per slide. The number of organisms surviving per treated slide subtracted from the number of organisms surviving on the control slides (treated with distilled water only) provides the % kill.

Table III summarizes typical results of these tests.

TABLE III
Bactericidal Activity on Non. Porous Surfaces
No. of Organisms Surviving/Slide After
Test
Germicide (cone-ppm) Organic Matte Organism 24 hrs. 48 hrs.

Q1 (50 ppm) 0.75% S. aureus - 1,080,000
Q1 (400 ppm) 2.0% " 79,000
Q1 (50 ppm) + 11 (25 ppm) 0.75% " - 6220
Q1 (400 ppm) + 12 (75 ppm) 2.0% " 20
Q1 (400 ppm) 2.0% E. aeroge. 175,500,000
Q1 (400 ppm) + 12 (75 ppm) 2.0% " 20 - Example IV.

Following the procedure of Example I, the following isothiazolones are evaluated in combination with quaternary Q1.

13-4 - bromo - 5 - chloro - 2 - n - propyl
3-isothiazolone 14-5 - chloro - 4 - methyl - 2 - phenyl
3-isothiazolone 15-4 - bromo - 5 - chloro - 2 - benzyl
3-isothiazoloen 16-4,5 - dichloro - 2 - n - hexyl - 3 - iso
thiazolone 17-2 - n - octyl - 3 - isothiazolone 18-5 - chloro - 2 - methyl - 3 - isothiazo
lone 19-2 - n - decyl - 3 - isothiazolone 110-5 - chloro - 4 - methyl - 2 - (3 - chloro
phenyl) - 3 - isothizolone
Table IV summarizes typical results of these tests.

TABLE IV
Time Survival Test

No. of Organisms Surviving
ml. of Test Solution After
Germicide (conc-ppm) Organic Matter 10 min. 30 min. 24 hr.

Q1 (400 ppm) 1% 500 280 < 100,000
Q1 (400 ppm) + 13 (50 ppm) 1% 46 0 0
Q1 (400 ppm) + 14 (50 ppm) 1% 0 0 0
Q1 (400 ppm) + 15 (50 ppm) 1% 83 0 0
Q1 (400 ppm) + 16 (50 ppm) 1% 0 0 0
Q1 (50 ppm) TNTC* TNTC TNTC
Q1 (50 ppm) + 17 (50 ppm) 0.25% TNTC* TNTC 2510
Q1 (50 ppm) + 18 (50 ppm) 0.25% TNTC* TNTC 0
Q1 (50 ppm) + 19 (50 ppm) 0.25% TNTC* TNTC 4
Q1 (50 ppm) + 110 (50 ppm) 0.25% 19250* 309 0 *After 15 minutes.

Example V.

When evaluated by the procedure of
Example 1, compositions combining other isothiazolones of Formula I, including
5 - chloro - 2 - n - octyl - 3 - isothiazolone
4 - bromo - 5 - chloro - 2 - (4 - chloro
phenyl) - 3 - isothiazolone
magnesium chloride comples of 2-methyl-5
chloro-3-isothiazolone 5 - chloro - 2 - methyl - 3 - isothiazolinium
chloride
calcium chloride complex of 4,5-dichloro
2-cyclohexyl-3-isothiazolone with typical bactericidal quatemary ammonium salts possess synergistic bactericidal activity.

Reference is directed to our copending
Application No. 21785/77 (Serial No.

1,488,892) which was divided from the present application and which claims a method of combating bacteria using, inter alia, the compositions of the present invention.

WHAT WE CLAIM IS:
1. A bactericidal composition containing a 3-isothiazolone and a bactericidal quaternary ammonium salt, wherein the 3-isothiazolone is (a) a compound of the formula: Formula (I) wherein
Y is (1) an optionally substituted alkyl group
(other than aralkyl), (2) a cycloalkyl group,
(3) an optionally substituted aralkyl group
or (4) (except in the case where R and R'
each represent chlorine) an optionally sub
stituted aryl group,
R is a hydrogen atom, a halogen atom, or an
optionally substituted alkyl group, and
R' is a hydrogen atom, a halogen atom, or an
optionally substituted alkyl group, (b) a salt of a compound of Formula I with an acid or (c) a metal salt complex of a compound of
Formula I.

2. A composition according to Claim 1 wherein, in Formula I, Y is (Cl-C,)alkyl, (Cl-Cs)cycolalkyl, phenyl optionally substituted by halogen or benzyl optionally substituted by halogen, R is hydrogen, halogen or (C1-C4)alkyl and R' is hydrogen or halogen.

3. A composition according to Claim 2, wherein Y is (CgC^)alkyl, (C3C)eyclo- alkyl, benzyl optionally substituted by bromine or chlorine, R is methyl, bromine or chlorine and R' is bromine or chlorine.

4. A composition according to Claim 3, wherein Y is alkyl or cycloalkyl each having six or seven carbon atoms.

5. A composition according to Claim 3, containing the calcium chloride complex of 5-chloro-2-methyl-3-isothiazolone.

6. A composition according to Claim 3, containing 4,5 - dichloro - 2 - cnclohexvl - 3isothiazolone.

7. A composition according to Claim 2, wherein R is (Cl-C)alkyl and R' is chlorine or bromine.

8. A composition according to Claim 7, containing 5 - chloro - 4 - methyl - 2 - 3 chiorophenyl) -3 - isothiazolone.

9. A composition according to Claim 1, containing a 3-isothiazolone which is any of the compounds identified in. foregoing
Example IV and V with the exclusion of the compound specified in Claim 8.

10. A composition according to Claim 1, wherein the 3-isothiazolone is a metal salt complex of the formula:

wherein
Y, R and R' are as defined in any of Claims
1-4 or 7,
M is a cation of a metal or a cationic complex
of a metal,
X is an anion forming a compound with the
cation M, wherein the compound has suf
ficient solubility to form a metal salt com
plex; a is the integer 1 or 2; and n is an integer which for the anion X satisfies
the valence of the cation M.

11. A composition according to Claim 10, wherein M is barium, cadmium, calcium, chromium, cobalt, copper, iron, lead, lithium, magnesium, manganese, mercury, nickel, sodium, silver, strontium, tin or zinc.

12. A composition according to any of the preceding claims wherein the weight ratio of the 3-isothiazolone to the quaternary ammonium salt is from 5:1 to 1:50.

13. A composition according to Claim 12, wherein said weight ratio is from 1:1 to 1:15.

14. A composition according to Claim 12, wherein said weight ratio is from 1:2 to 1:7.

15. A composition according to any of the preceding claims wherein the quaternary ammonium salt has at least one hydrophobic aliphatic claim of 8 to 18 carbon atoms.

16. A composition according to Claim 15, wherein the quaternary ammonium salt is a di(C1-C4)alkyl (C8-C18)alkyl benzyl ammonium halide.

17. A composition according to Claim 16, wherein the quaternary ammonium salt is at least one n-(C,-Cl)alkyl dimethyl benzyl ammonium halide.

18. A composition according to Claim 17, wherein the quaternary ammonium salt is a mixture of

n-Cl2alkydimethylbenzyl ammonium chloride, n-Clsalkyldimethylbenzyl- ammonium chloride and n-Cl,.alkyldimethyl- benzylammonium chloride.

WARNING end of DESC field may overlap start of CLMS **.

1,488,892) which was divided from the present application and which claims a method of combating bacteria using, inter alia, the compositions of the present invention.

WHAT WE CLAIM IS:

1. A bactericidal composition containing a 3-isothiazolone and a bactericidal quaternary ammonium salt, wherein the 3-isothiazolone is (a) a compound of the formula:

Formula (I) wherein
Y is (1) an optionally substituted alkyl group
(other than aralkyl), (2) a cycloalkyl group,
(3) an optionally substituted aralkyl group
or (4) (except in the case where R and R'
each represent chlorine) an optionally sub
stituted aryl group,
R is a hydrogen atom, a halogen atom, or an
optionally substituted alkyl group, and
R' is a hydrogen atom, a halogen atom, or an
optionally substituted alkyl group, (b) a salt of a compound of Formula I with an acid or (c) a metal salt complex of a compound of
Formula I.

2. A composition according to Claim 1 wherein, in Formula I, Y is (Cl-C,)alkyl, (Cl-Cs)cycolalkyl, phenyl optionally substituted by halogen or benzyl optionally substituted by halogen, R is hydrogen, halogen or (C1-C4)alkyl and R' is hydrogen or halogen.

3. A composition according to Claim 2, wherein Y is (CgC^)alkyl, (C3C)eyclo- alkyl, benzyl optionally substituted by bromine or chlorine, R is methyl, bromine or chlorine and R' is bromine or chlorine.

4. A composition according to Claim 3, wherein Y is alkyl or cycloalkyl each having six or seven carbon atoms.

5. A composition according to Claim 3, containing the calcium chloride complex of 5-chloro-2-methyl-3-isothiazolone.

6. A composition according to Claim 3, containing 4,5 - dichloro - 2 - cnclohexvl - 3isothiazolone.

7. A composition according to Claim 2, wherein R is (Cl-C)alkyl and R' is chlorine or bromine.

8. A composition according to Claim 7, containing 5 - chloro - 4 - methyl - 2 - 3 chiorophenyl) -3 -isothiazolone.

9. A composition according to Claim 1, containing a 3-isothiazolone which is any of the compounds identified in. foregoing
Example IV and V with the exclusion of the compound specified in Claim 8.

10. A composition according to Claim 1, wherein the 3-isothiazolone is a metal salt complex of the formula:

wherein
Y, R and R' are as defined in any of Claims
1-4 or 7,
M is a cation of a metal or a cationic complex
of a metal,
X is an anion forming a compound with the
cation M, wherein the compound has suf
ficient solubility to form a metal salt com
plex; a is the integer 1 or 2; and n is an integer which for the anion X satisfies
the valence of the cation M.

11. A composition according to Claim 10, wherein M is barium, cadmium, calcium, chromium, cobalt, copper, iron, lead, lithium, magnesium, manganese, mercury, nickel, sodium, silver, strontium, tin or zinc.

12. A composition according to any of the preceding claims wherein the weight ratio of the 3-isothiazolone to the quaternary ammonium salt is from 5:1 to 1:50.

13. A composition according to Claim 12, wherein said weight ratio is from 1:1 to 1:15.

14. A composition according to Claim 12, wherein said weight ratio is from 1:2 to 1:7.

15. A composition according to any of the preceding claims wherein the quaternary ammonium salt has at least one hydrophobic aliphatic claim of 8 to 18 carbon atoms.

16. A composition according to Claim 15, wherein the quaternary ammonium salt is a di(C1-C4)alkyl (C8-C18)alkyl benzyl ammonium halide.

17. A composition according to Claim 16, wherein the quaternary ammonium salt is at least one n-(C,-Cl)alkyl dimethyl benzyl ammonium halide.

18. A composition according to Claim 17, wherein the quaternary ammonium salt is a mixture of n-Cl2alkydimethylbenzyl ammonium chloride, n-Clsalkyldimethylbenzyl-ammonium chloride and n-Cl,.alkyldimethyl- benzylammonium chloride.
